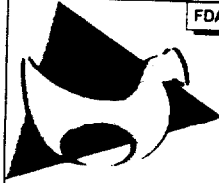


FDA/ENC Sept. 8, 2000



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Applications

- **Vaccine development**
- **Development of science-based regulations for better control**
- **Improved epidemiological monitoring**



***Topics in Microbial Pathogenesis
With Special Relevance to Egg
Contamination by SE***

- **Outer membrane complex
carbohydrates (mainly LPS)**
- **High cell density growth
(quorum sensing)**
- **Proteotomes (changes in surface
proteins in response to
environmental stimuli)**

<div>  <div> <div>FDA/ENC Sept.8, 2000</div> <div> <i>Relative contribution of virulence factors to egg contamination</i> </div> </div> </div>			
20 day old chicks (8-10 per treatment)			
strain	route of challenge	% spleens positive (number positive/number cultured)	average CFU/ positive spleen
wildtype	oral	60 (6/10)	4×10^1
	SQ	100 (8/8)	1×10^4
<i>fliC::Tn10</i>	oral	60 (6/10)	8×10^1
	SQ	100 (8/8)	2×10^3
<i>fliH::Tn10</i>	oral	89 (8/9)	5×10^3
	SQ	100 (8/8)	5×10^2
<i>sipD::Tn10</i>	oral	0 (0/10)	0
	SQ	100 (9/9)	2×10^4

RESULTS:

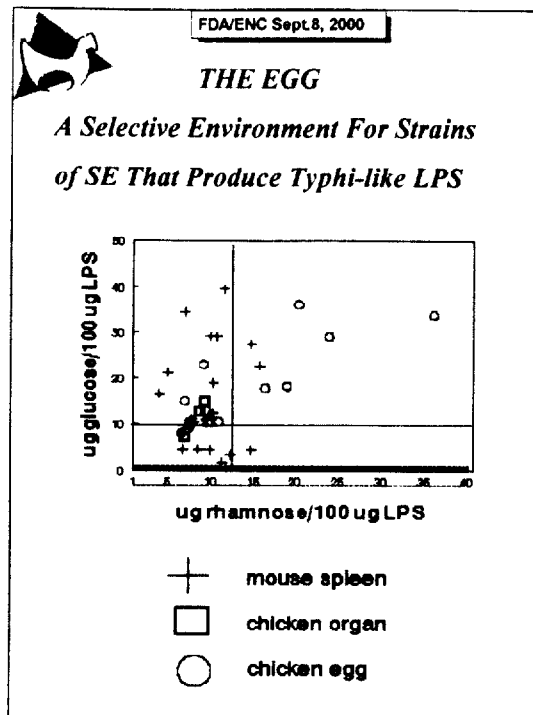
SipD required for oral invasion, not for high cell density growth in organs.
 Flagellation generally required for high cell density growth, not oral invasion.
 Some types of flagellation mutants appear to have enhanced oral invasion.

DISCUSSION:

Oral invasion is separate process from high cell density growth in organs.
 Each virulence compartment could require a different approach to achieve immunization.
 Results provide a framework for understanding how *S. pullorum* could have lost flagellation while remaining virulent.

FUTURE RESEARCH:

Investigate environmental stimuli that alter production of SIP and flagella.
 Determine how often and under what conditions SE strains resemble *S. pullorum* (flagella-, motility-).



Characterization of LPS structures from SE isolates recently isolated from naturally infected mice caught in hen houses, organs of chickens and eggs.

RESULTS:

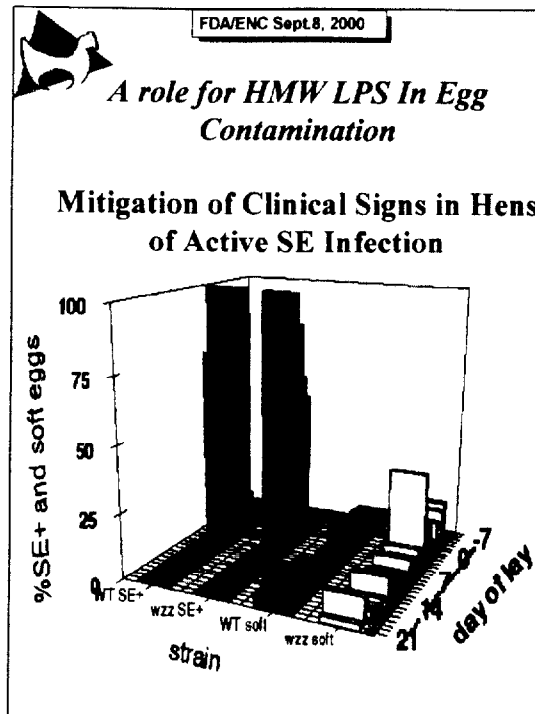
The egg is the richest source for SE isolates that produce Typhi-like LPS.

Isolates from mice produce a wide variety of LPS structures, especially non-glucosylated forms.

Organs of chickens (spleen, kidney, liver pool) yield a LPS structure typical of other paratyphoid salmonellae (such as *S. typhimurium*), but more samples need to be processed to see if the variance in structure is as low as it appears here.

DISCUSSION

SE isolates that result in egg contamination often produce Typhi-like LPS (glucosylated HMW LPS).



LEGEND:

Red bars = challenge of hens with SE wildtype

(parameter measured is egg contamination).

Blue bars = challenge of hens with wzz SE, which lacks HMW-LPS

(parameter measured is egg contamination)

Purple bars = challenge of hens with SE wildtype

(parameter measured is eggshell quality)

Yellow bars = challenge of hens with wzz SE, which lacks HMW-LPS

(parameter measured is eggshell quality)

RESULTS:

At the dosage examined , 10^7 CFU administered intravenously, about 10% of eggs in each group (3 week clutch) were contaminated.

Only the mutant resulted in poor quality eggshells associated with egg contamination.

DISCUSSION:



Typhoid Fever Model

- **Low infectious dose (10 CFU)**
 - **Lowest dosage for SE human illness is 28 CFU**
- **Septicemia and deeper tissue infections are commonly reported in people.**
- **Gastroenteritis is not often a presenting sign**
 - **Collapse from anemia (bleeding into gut often reported as constipation) and high fever are prominent.**



APPLIED RESEARCH NEEDS

- **Modify technology to assess shell quality (perhaps laser air puff equipment)**
- **Identify parameters that might alter or maximize eggshell quality differences (experimental hen challenge model)**
- **Establish parameters of eggshell quality of eggs at market using state of the art technology**